AMENDMENTS TO THE CLAIMS

1. (original) A method of preparing the chiral (±) isomers of indole-2,3-dione-3-oxime derivatives (Compounds A or B), which method comprises the subsequent steps of

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline (Compound 9) derivative with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide (Compound 10) derivative (Step 9);

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide (Compound 10) derivative obtained in step (i) (Step 10); and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline (Compound 11) derivative obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid) (Compound A or B) (Step 11);

followed by recovery of the desired end product.

2. (original) The method of claim 1, which method further comprises the step of

(a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone (Step 8a);

followed by steps (i) to (iii) of claim 1.

3. (currently amended) The method of claim 1 [[2]], which method further comprises the step of

(b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc-hydroxylamine (Step 7);

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone (Step 8a); ~~of claim 2,~~ and

followed by steps (i) to (iii) of claim 1.

4. (currently amended) The method of claim 1 [[3]], which method further comprises the step of

(c) converting *O*-benzylhydroxylamine into *N,N*-diBoc-*O*-benzylhydroxylamine using Boc_2O (Step 6);

followed by step (b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc-hydroxylamine (Step 7); ~~of claim 3,~~

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone (Step 8a); ~~of claim 2,~~ and

followed by steps (i) to (iii) of claim 1.

5. (currently amended) The method of claim 1, which method further comprises the step of

(d) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with tosyl chloride to give enantiopure (*S*) or (*R*) α-tosyloxy-γ-butyrolactone (Step 5);

followed by step (c) converting *O*-benzylhydroxylamine into *N,N*-diBoc-*O*-benzylhydroxylamine using Boc_2O (Step 6); ~~of claim 4,~~

followed by step (b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc-hydroxylamine (Step 7); ~~of claim 3,~~

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone (Step 8a); ~~of claim 2,~~ and

followed by steps (i) to (iii) of claim 1.

6. (previously presented) The method of claim 1, wherein

the 8-amino-1,2,3,4-tetrahydro-isoquinoline (Compound 9) derivative of step (i) is 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-5-yl)-*N,N*-dimethyl-benzenesulfonamide (to

obtain *N*-[5-(4-dimethylsulfamoyl-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-yl]-2-hydroxyimino-acetamide); and

the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline (Compound 11) derivative of step (iii) is *N,N*-dimethyl-4-(8-methyl-2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinolin-5-yl)-benzenesulfonamide;

giving enantiopure (R)- or (S)-2-[5-(4-dimethylsulfamoyl-phenyl)-8-methyl-2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid as the end product (Compound A or B).

7. (previously presented) A method of preparing a starting material for use according to the method of claim 1, which method comprises the subsequent steps of

(i) acetylating a racemic mixture of α-hydroxy-γ-butyrolactone to obtain racemic α-acetoxy-γ-butyrolactone (Step 1);

(ii) subjecting the racemic α-acetoxy-γ-butyrolactone obtained in step (i) to enzymatic de-acetylation to obtain enantiopure (*S*) or (*R*) α-acetoxy-γ-butyrolactone (Step 2); and

(iii) subjecting the enantiopure (*S*) or (*R*) α-acetoxy-γ-butyrolactone obtained in step (ii) to hydrolysis using acidic ion-exchange (Step 3);

followed by recovery of the desired end product.

8. (original) The method of claim 7, which method further comprises the step of

(iv) subjecting the enantio-impure remainings of step (iii), i.e. the enantio-impure α-hydroxy-γ-butyrolactone and α-acetoxy-γ-butyrolactone, to racemisation using acid or base; followed by re-entry of the racemic mixture into step (i).

9. (original) The method of claim 7, wherein the enzymatic de-acetylation of step (ii) is carried out using a lipolytic enzyme.

10. (previously presented) Enantiopure (R)-2-[5-(4-dimethylsulfamoyl-phenyl)-8-methyl-2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

11. (previously presented) Enantiopure (S)-2-[5-(4-dimethylsulfamoyl-phenyl)-8-methyl-2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.